REMARKS

Claims 11-25, 27-30, 32-34, and 36-58 remain pending. By the foregoing amendment, claims 31 and 35 have been cancelled and independent claim 11 has been amended to point out that moxifloxacin or a pharmaceutically useful hydrate or salt thereof is present in a concentration of 0.1 to 1.0 wt. %. Support for the amendment is found in the specification, *e.g.*, at page 7, lines 14-16, and this limitation appeared in previously-entered claim 26, which has been cancelled. Claims 36, 38, 40, 41, 43-45, 49, and 51 have been amended to change their dependencies. Claims 37 and 55 have been amended to point out that the composition contains at least one of a viscosity enhancing agent and a surfactant. No new matter is added.

The courtesy extended by the Examiner at the interview of May 2, 2007 is gratefully acknowledged. The following is a summary of the matters presented at the interview with reference to materials already of record as well as the Stroman Declaration submitted herewith.

Background of the Invention

- Antibiotics are applied prophylacticly during eye surgery, with a key focus on combating *Pseudomonas aeruginosa*, a dangerous ocular pathogen relative to infections that may cause a loss of sight (Stroman Declaration, ¶ 9(a)).
- Prior commercial formulations employed other quinolones, with ciprofloxacin and ofloxacin considered to be the state of the art.
- At the time of invention, moxifloxacin was reported to be 2 to 8-fold ***less active*** than ciprofloxacin against *P. aeruginosa* in *in vitro* testing (Woodcock et al., *Antimicrobial Agents and Chemotherapy*, American Society of Microbiology, Jan. 1997).

The Invention

- The invention of claim 11 is directed to a method of treating ophthalmic infections by topically applying to the eye a pharmaceutical composition containing moxifloxacin or a pharmaceutically useful hydrate or salt thereof.
- An embodiment of the present invention formulated as an ophthalmic solution containing 0.5 wt. % moxifloxacin (i.e., Alcon's VIGAMOX®) has achieved very significant commercial success, reaching total global sales of $ 100,000,000 in its first full year of sales (2004) and global sales of $ 185,000,000 in 2006. (Stroman Declaration ¶ 21).
- Work by the present inventors yielded the surprising discovery that moxifloxacin, when administered topically to the eye in accordance with the compositions and methods of the present invention, is characterized by unexpected ocular penetration properties that enhance its ability to treat ophthalmic infections. (Stroman Declaration ¶ 13).

Rejection Under 35 U.S.C. § 102

Claim 11 stands rejected under 35 U.S.C. § 102(b) as being anticipated by Petersen et al. U.S. Patent 5,607,942 ("Petersen"). This rejection is respectfully traversed.

Petersen is cited as describing moxifloxacin in claim 2 and the treatment of eye infections at column 54. Petersen actually discloses 151 compounds in Table I and 53 indications in column 54, which amounts to more than 8,000 treatment combinations of quinolone structures and infections. As Judge Rich explained in *In re Ruschig*, 379 F.2d 990, 994, 154 U.S.P.Q. 118 (C.C.P.A. 1967), "something more than the disclosure of a class of 1000, or 100, or even 48" is needed for a generic disclosure to describe a species. The court in *In re Arkley*, 455 F.2d 586, 587, 172 U.S.P.Q. 524 (C.C.P.A. 1972), held an anticipation rejection requires that a prior art

reference "clearly and unequivocally disclose" the claimed subject matter "without *any* need for picking, choosing, and combining various disclosures" in the reference. (emphasis in original).

Quinolones have widely varying activities and uses, and Petersen refers not only to 53 human indications for use, but also some 34 additional indications for animals. Moxifloxacin is not singled out for any particular indication in claim 2 or in the specification. Moreover, Petersen provides no biological data for moxifloxacin, which casts further doubt on the indications for which it might actually be useful.

In any event, claim 11 has been amended to recite a therapeutically effective amount within a concentration of 0.1 to 1.0 wt. %, a recitation that already appeared in claim 26 and that removes claim 11 even further from the Petersen disclosure. Dependent claim 28 (concentration of greater than 0.1 wt. %), dependent claim 29 (at least 0.35 wt. %), and dependent claim 30 (about 0.35 wt. %) are yet further removed from Petersen.

Rejection Under 35 U.S.C. § 103

Claims 12-58 stand rejected under 35 U.S.C. § 103(a) as being obvious over Petersen in view of Cagle et al. WO 90/01933 ("Cagle '933") and Bergamani et al. U.S. Patent 5,597,560 ("Bergamani"). This rejection is respectfully traversed.

Cagle '933 and Bergamani are cited as describing the use of steroidal and non-steroidal anti-inflammatory agents in ophthalmic formulations, respectively. Cagle '933 and Bergamani fail to remedy the deficiencies of Petersen as discussed above. Dependent claims 12-25, 27-30, 32-34, and 36-58 are allowable over Petersen, Cagle '933, and Bergamani for at least the same reasons as argued above.

Additional reasons support the non-obviousness of the claimed invention. As discussed above, the art as a whole taught away from selecting moxifloxacin for treating ophthalmic

infections because it was acknowledged to be inferior to the existing state of the art (i.e., ciprofloxacin) in terms of its *in vitro* activity against *P. aeruginosa*, a dangerous ocular pathogen. See Woodcock et al., *Antimicrobial Agents and Chemotherapy*, American Society of Microbiology, Jan. 1997, as well as paragraphs 10-12 of the Stroman Declaration.

Moxifloxacin's superior ocular penetration properties were unexpected. The superior ocular penetration properties of moxifloxacin have been confirmed by third parties. A review of numerous published scientific articles wherein the ocular bioavailability of moxifloxacin and other fluoroquinolones when administered via ophthalmic compositions is provided in a Special Supplement to the November, 2005 edition of Survey of Ophthalmology, International Review Journal (volume 50, supplement 1). The review article was authored by Alcon scientists, but the studies reviewed in the article were conducted by a variety of personnel, including both Alcon scientists and other scientists. The overall significance of the results of the studies is summarized on page S32 of the Supplement as follows:

> The results consistently demonstrate higher maximum concentrations for moxifloxacin relative to the other fluoroquinolones in ocular tissues with levels well above its minimum inhibitory concentrations for relevant ocular pathogens ... It is clear from the array of studies summarized in this report that moxifloxacin penetrates ocular tissues better (two to three-fold) than gatifloxacin, ciprofloxacin, ofloxacin, levofloxacin. This consistent, enhanced penetration of topical moxifloxacin offers powerful advantages for ophthalmic therapy.

Moxifloxacin demonstrated from over 2 to over 10 times the MDCK permeability and from over 2 to over 10 times the corneal permeability of other quinolones. (Id. at S36). As demonstrated in the Stroman Declaration, the unexpected ocular penetration properties of moxifloxacin will be seen throughout the claimed range of 0.1 – 1.0 wt. %. (Stroman Declaration ¶¶ 17-20).

Topical ophthalmic formulations containing moxifloxacin were determined to be patentable over Petersen on at least two significant occasions before:

1) The present applicants were awarded U.S. Patent 6,716,830 containing a claim to a topical ophthalmic pharmaceutical composition comprising 0.1 to 1 wt% moxifloxacin or a pharmaceutically useful hydrate or salt thereof. Petersen was considered during that prosecution.

2) A third party relied on Petersen in an opposition to the European counterpart of the present application. After full briefing and an oral argument, the three member Opposition Panel rejected the opposition to the claim directed to a topical ophthalmic composition comprising 0.1 to 1.0 wt % moxifloxacin. (See EPO Decision dated October 30, 2006).

The Office Action asserts that moxifloxacin's ocular penetration is an inherent property that cannot distinguish the prior art, citing *In re Best*, 562 F.2d 1252, 195 U.S.P.Q. 430 (C.C.P.A. 1977), and *In re Fitzgerald*, 619 F.2d 67, 205 U.S.P.Q. 594 (C.C.P.A. 1980). However, the reliance on these decisions in the Office Action is misplaced because both require that the prior art "expressly disclose" all claim limitations. *Best*, 195 U.S.P.Q. at 432. As discussed above, Petersen does not describe administering moxifloxacin in any formulation expressly for treating ophthalmic infections. The presently amended claims, with concentration ranges and other limitations, are not anticipated or rendered obvious by Petersen.

CONCLUSION

None of the prior art documents, whether taken alone or in any combination, describes or suggests the method of claims 11-25, 27-30, 32-34, and 36-58. Reconsideration and withdrawal of the §§ 102 and 103 rejections are respectfully requested.

Applicants appreciate Examiner Fay's indication that she will contact the undersigned by telephone in the event any issues arise in her consideration of this response. Prompt issuance of a Notice of Allowance is earnestly solicited.

Respectfully submitted,
BANNER & WITCOFF, LTD.

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By: /Paul M. Rivard/
Paul M. Rivard
Registration No. 43,446

1100 13th Street N.W.
Suite 1200
Washington, DC 20005-4051
(202) 824-3000 (telephone)
(202) 824-3001 (facsimile)